

REMARKS

Claims 2, 3, 5, 7, 8, 39-43, and 45-57 and 59-68 are pending in the application.

Applicants have canceled claims 6 and 58 and reserve the right to pursue the subject matter of

these claims in a continuation application. Applicants have amended claims 2, 42 and 53.

Support for the amendments to claims 2 and 42 can be found, for example, in claims 6 and 58 as previously presented. No new matter is added.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner maintained the rejection of claims 2, 3, 5-8, 39-43 and 45-68 under 35 U.S.C. § 112, first paragraph for lack of enablement and lack of written description. In response, Applicants have amended the claims and traverse this rejection for the reasons explained below.

Claims 2 and 53, from which the remaining claims subject to the rejection depend, recite a method for modulating activation of an NF κ B signaling pathway by contacting a cell having TRADE activity with the extracellular domain of a TRADE α polypeptide.

Applicants have amended claims 2 and 53 to stipulate that the TRADE peptide must be a soluble form and to require that modulation of NF κ B activation results in a modulation of proliferation of the cell. Soluble forms of the TRADE polypeptide can be used as TRADE ligand antagonists.¹ Soluble TRADE peptides comprising the extracellular portion of the TRADE protein act as antagonists to TRADE ligand.² This antagonism of TRADE ligand leads to change in the activity of the intracellular portion of the TRADE proteins expressed in a cell to which the soluble TRADE extracellular portion is administered to. As described in Example 4 of the

¹ See the instant specification at page 49, lines 15-19.

² *Id.* from page 130, line 17 to page 131, line 6.

instant application, modulation of the activity of the intracellular portion of the TRADE protein will lead to modulation of NFkB activity.

Applicants submit that the disclosure of the instant application is sufficiently enabling to claims 2, 3, 5-8, 39-43 and 45-68 and respectfully request that this rejection be withdrawn.

The Examiner also rejected claims 2, 3, 5-8, 39-43, and 45-68 under 35 U.S.C. § 112, first paragraph as having new matter. The rejection is traversed to the extent it is applied to the claims as amended.

The apparent basis for the Examiner's rejection is that the specification does not support a method of modulating activation of an NJkB signaling pathway in call comprising contacting a cell having TRADE activity with a TRADE activity, wherein the TRADE polypeptide comprises the extracellular domain of a TRADE α polypeptide. Applicants submit that support for these features of the claimed method appears in at least the original claims of the application.

Original claims 15, 16, 18-20 and 25 of the application recite as follows (emphasis added):

15. A method of modulating the proliferation of a cell comprising contacting the cell with an agent that modulates the expression of a TRADE family member polypeptide, wherein the cell is selected from the group consisting of an epithelial cell, a ductal epithelial cell, a carcinoma cell, and an adenocarcinoma cell, such that the proliferation of the cell is modulated.

16. A method of modulating the proliferation of a cell comprising contacting the cell with an agent that modulates the activity of a TRADE family member polypeptide, wherein the cell is selected from the group consisting of: an epithelial cell, a ductal epithelial cell, a carcinoma cell, and an adenocarcinoma cell such that the proliferation of the cell is modulated.

18. The method of claim 15 or 16, wherein the agent is a soluble form of a TRADE family polypeptide comprising a TRADE extracellular domain.

19. The method of claim 18, wherein the soluble form of a TRADE family polypeptide is a TRADE-Fc fusion protein.

20. The method of claim 15 or 16, wherein the agent consists essentially of a TRADE family extracellular domain.

25. The method of claim 16, wherein the activity is selected from the group of activities consisting of: *activation of a JNK signaling pathway*, activation of an NFkB signaling pathway, and activation of apoptosis.

Thus, claims 15 and 16, and the dependent claims noted above, support a method that includes modulating activation of an NJkB signaling pathway in call bycontacting a cell having TRADE activity with a TRADE activity, wherein the TRADE polypeptide comprises the extracellular domain of a TRADE α polypeptide

Applicants respectfully request reconsideration and withdrawal of the rejection for lack of written description.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has also rejected claims 2, 3, 5-8, 39-43, 45-52, 66 and 67, under 35 U.S.C. § 112, second paragraph, for indefiniteness. The Examiner alleged that claim 2 was indefinite for reciting, "said extracellular domain corresponding to a polypeptide and that claim 42 was rejected for reciting, "a polypeptide sequence at least encoded by a polynucleotide sequence..." Applicants have amended claim 2 to delete the phrase "corresponding to" and have amended claim 42 to delete the phrase "at least" before "encoded by". Applicants submit that claims 2, 3, 5-8, 39-43, 45-52, 66 and 67 are definite and respectfully request that this rejection be withdrawn.

Applicants submit the application is in condition for allowance, and request an action for same. A petition for a extension of time accompanies this response. Please charge any additional fees due or credit any overpayment of same to the undersigned's Deposit Account No. 50-0311, Reference No. 22058-569.

Respectfully submitted,

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